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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/400,769	09/22/1999	ERIK HELMERHORST	28594/35007A	3787

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EXAMINER	
ROBINSON, HOPE A	

ART UNIT	PAPER NUMBER
1653	31

DATE MAILED: 08/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/400,769	HELMERHORST ET AL.	
	Examiner	Art Unit	
	Hope A. Robinson	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the corresp ndence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-10,16,17,20-25 and 32-47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-10,16,17,20-25 and 32-47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *27* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Applicant's response to the Office Action mailed November 29, 2002 in Paper Nos. 26-30 on April 7, 2003, May 13, 2003, May 21, 2003 and June 3, 2003 is acknowledged.

Claim Disposition

2. Claims 11-15, 18-19 and 26-31 have been canceled. Claims 32-47 have been added. Claims 1-4, 6 and 16 have been amended. Claims 1-10, 16-17, 20-25, 32-47 are pending and under examination.

3. The following grounds of rejection are or remain applicable:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-10, 16-17, 20-25, 32-47 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for agonist and antagonist of insulin, does not reasonably provide enablement for one agonist that would treat a patient suffering from both hypoglycemia and hyperglycemia or one antagonist that would treat a patient suffering from both hypoglycemia and hyperglycemia. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. These factors include, but are not limited to:

I. Quantity of Experimentation Necessary:

The claimed invention is directed to a method for treating a patient suffering from one or more insulin related ailments selected from the group consisting of hyperglycemia, hypoglycemia, diabetes mellitus, insulinomas, insulin and hypoglycemic drug overdoes, gastric dumping syndrome, congenital hyperinsulinism and Alzheimer's disease. The specification on page 2 indicates that an agent that has stimulatory activity is termed an agonist and an agent that inhibits is termed antagonists. However, the specification does not demonstrate or provide any information regarding an agonist or antagonist having the activity of affecting a hyper and hypoglycemic condition. Thus there is no demonstration of one compound having two opposing activity with regard to treating hyper and hypo-glycemia. Therefore, one of ordinary skill in the art would have

to engage in undue experimentation to be to determine if the compounds are partial agonist/antagonist.

II. Amount of direction or guidance presented:

The specification on pages 55+ provides a list of compounds that are designated as antagonist and agonist of insulin action, and the list of compounds do not overlap to indicate that a single compound has the activity of being an agonist and antagonist. However, the claims recite that the disease of hyperglycemia (too much sugar) and hypoglycemia (too little sugar) can be treated by an agonist alone or antagonist alone, thus implying that a single compound has both antagonistic and agonistic properties. Therefore, absent adequate guidance one of skill in the art would not be able to practice the invention commensurate in scope with the claims because it is unclear if the compounds of the claimed invention can act as both agonist and antagonist.

III. Presence or absence of working examples:

No working examples are provided that demonstrate a compound having agonistic and antagonist activity commensurate in scope with the claims.

IV. Nature of the Invention:

The invention requires a compound that is an agonist for treatment of hyperglycemia and hypoglycemia, and a compound that is an antagonist for treatment of hyperglycemia and hypoglycemia, however, no such compound is demonstrated in the instant specification. The specification on page 55 lists the following antagonist compounds: IM 025, IM 071, IM 127, IM 129, IM 132, IM 134, IM 143, IM 144, IM 145, IM 171 and IM 172 and the following agonist compounds: IM 140, IM 175, IM 103 (see page 63), therefore, no compound appear to have both agonist and antagonistic activity, as such, the specification needs to provide guidance to indicate how hyperglycemia and hypoglycemia are being treated with a compound that is solely and agonist or antagonist.

V. State of the prior art and Relative skill of those in the art/Predictability or unpredictability of the art:

The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Additionally, no analogous art was found; therefore, the art is unpredictable.

VII. Breadth of the claims:

The claims encompass compounds that would be both agonist and antagonist, however, there is no demonstration of the two opposing activity in the instant specification in association with the recited diseases/disorders.

Thus, for all these reasons, the specification is not considered to be enabling for one skilled in the art to make and use the claimed invention commensurate in scope with the claims.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-10, 16-17, 20-25, 32-47 are rejected under 112, second paragraph as failing to distinctly point out the subject matter applicant regards as his invention. Claim 1 as amended is indefinite because the Markush language is improper, where the claim recites "selected from the group consisting of hyperglycemia, hypoglycemia, diabetes mellitus, insulinomas, insulin and hypoglycemic drug overdose, gastric dumping syndrome and congenital hyperinsulinism, Alzheimer's disease...", the claim should be rewritten as "selected from the group consisting of hyperglycemia, hypoglycemia, diabetes mellitus, insulinomas, insulin hypoglycemic drug overdose, gastric dumping syndrome, [and]congenital hyperinsulinism [,] and Alzheimer's disease..." (see also claim 32). The dependent claims are also included in this rejection.

Claims 8, 21, 23, 24, 39, 43, 45 and 46 are indefinite for the recitation of a Markush listing that ends with "or" instead of "and", for example the Markush listing should consists of "selected from the group consisting of A, B and C".

Claim 20 is indefinite because the claim recites improper Markush language, where there appears "selected from the group consisting of: benzene, pyridine, pyridazine, pyrimidine, pyrazine, triazine" which should be rewritten as "selected from the group consisting of: benzene, pyridine, pyridazine, pyrimidine, pyrazine and triazine" (see also claims 22, 25, 42, 44 and 47).

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

6. The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

7. Claims 1-3 and 16-17 are rejected under 35 U.S.C. 102(a) as being anticipated by Sportsman et al. (U.S. Patent No. 5,851,988, December 22, 1998).

Sportsman et al. teach a method for controlling and managing diabetes mellitus with an insulin agonist (non-peptidyl compound that has ionic and hydrophobic chemical moieties spatially located so as to mimic insulin (claim 1)). As the reference teaches a compound that mimics insulin with one or more ionic residues and hydrophobic residues claims 2 and 3 are anticipated (see abstract, figures 2, 3, 5 and 9, and columns 1-3). The methods of claims 16 and 17 are anticipated because the reference describes methods in columns 2-3, to design and synthesize a molecule that exhibits agonist activity or insulin agonist stimulating activity with respect to the insulin receptor comprising assessing the structural features which correlate with such said activities and doing a comparison study, and to screen candidate compounds for the ability to activate the insulin receptor. Thus, the limitations of the claims are met by this reference.

8. Claims 1-3 and 16-17 are rejected under 35 U.S.C. 102(a) as being anticipated by Sportsman et al. (U.S. Patent No. 6,329,431, August 21, 1997).

Sportsman et al. a method for controlling and managing diabetes mellitus with an insulin agonist (non-peptidyl compound that has ionic and hydrophobic chemical moieties spatially located so as to mimic insulin (claim 1). As the reference teaches a compound that mimics insulin with one or more ionic residues and hydrophobic residues claims 2 and 3 are anticipated (see abstract, figures 2, 3, 5 and 9, and columns 1-3). The methods of claims 16 and 17 are anticipated because the reference describes methods in columns 2-3, to design and synthesize a molecule that exhibits agonist activity or insulin agonist stimulating activity with respect to the insulin receptor

comprising assessing the structural features which correlate with such said activities and doing a comparison study, and to screen candidate compounds for the ability to activate the insulin receptor. Thus, the limitations of the claims are met by this reference.

9. Applicant's arguments filed on April 7, 2003 have been fully considered. Note that the rejections of record have been withdrawn, however, based on the amendments to the claims new grounds of rejections have been instituted. It is noted that applicant implemented the suggested language into the claims to obviate the grounds of rejection under 35 U.S.C. 112, second paragraph, however, each amendment warrants a new search, hence the cited prior art above. Note also the new grounds of rejection under 35 U.S.C. 112, second paragraph for the reasons stated above.

Conclusion

10. No claims are allowable.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Hope A. Robinson whose telephone number is (703)308-6231. The Examiner can normally be reached on Monday- Friday from 9:00 A.M. to 5:30 P.M. (EST).

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor Christopher S.F. Low, can be reached at (703)308-2932.

Any inquiries of a general nature relating to this application should be directed to the Group Receptionist whose telephone number is (703)308-0196.

Papers related to this application may be submitted by facsimile transmission. The official fax phone number for Technology Center 1600 is (703) 308-2742. Please affix the Examiner's name on a cover sheet attached to your communication should you choose to fax your response. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (November 15, 1989).

Hope A. Robinson, MS

Patent Examiner

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